PATENT
ATTORNEY DOCKET NO. 50294/016001

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| Applicant: | Tedesco et al. | Art Unit: | 1644 |
| Serial No.: | 10/521,109 | Examiner: | Francois P. Vandervegt |
| Filed: | January 11, 2005 | Customer No.: | 21559 |
| Confirmation No.: | 5428 | | |
| Title: | Antibodies Anti-C5 Component of the Complement System and Their Use | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO CORRECT FILING RECEIPT

Applicants request that the enclosed filing receipt be corrected as follows.

Please add the following under the heading "Foreign Applications":

ITALY MI2002A001527 7/11/2002.

Enclosed are copies of the incorrect filing receipt and Declaration of the Inventors, which indicate the priority claim to the Italian application as is noted above. Also enclosed is a copy of a Preliminary Amendment that was filed with the application and adds the priority claim to the specification, including that above-noted Italian application (as well as the priority claim to the PCT application). Applicants further note that the application transmittal letter (a copy is enclosed) indicates that the priority date claimed is July 11, 2002, the filing date of the Italian application noted above. Applicants also submit herewith an Application Data Sheet including this information. A petition to make this correction was previously filed, but Applicants have not received a Corrected Filing Receipt.

Although no charges are believed to be due, if there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: March 9, 2007

Susan M. Michaud, Ph.D.
Reg. No. 42,885

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045

DE-DOCKETED

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| APPL NO. | FILING OR 371 (c) DATE | ART UNIT | FIL FEE REC'D | ATTY.DOCKET NO | DRAWINGS | TOT CLMS | IND CLMS |
|---|---|---|---|---|---|---|---|
| 10/521,109 | 01/11/2005 | 2183 | 1950 | 50294/016001 | 11 | 40 | 13 |

**CONFIRMATION NO. 5428**

21559
CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

**FILING RECEIPT**
*OC000000016886904*
*OC000000016886904*

Date Mailed: 08/31/2005

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please mail to the Commissioner for Patents P.O. Box 1450 Alexandria Va 22313-1450. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

**Applicant(s)**

Francesco Tedesco, Trieste, ITALY;
Roberto Marzari, Trieste, ITALY;

**Power of Attorney:** The patent practitioners associated with Customer Number **21559**.

**Domestic Priority data as claimed by applicant**

This application is a 371 of PCT/EP03/07487 07/10/2003

**Foreign Applications**

Italy MI2002A001527 07/11/2002

**Projected Publication Date:** 12/08/2005

**Non-Publication Request:** No

**Early Publication Request:** No

**** SMALL ENTITY ****

**Title**

Antibodies anti-c5 component of the complement system and their use

**Preliminary Class**

712

## PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

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**Box No. VIII (iv) DECLARATION: INVENTORSHIP (only for the purposes of the designation of the United States of America)**

*The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (v) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.*

**Declaration of inventorship (Rules 4.17(iv) and 51*bis*.1(a)(iv)) for the purposes of the designation of the United States of America:**

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/EP03/07487 (if furnishing declaration pursuant to Rule 26*ter*).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications: Italy Appln. No. MI2002A001527 of 11 July 2002

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

**Name:** Francesco TEDESCO

Residence: TRIESTE – ITALY
(city and either US state, if applicable, or country)

Mailing Address: Via De Guardi 3 – 34143 TRIESTE – ITALY

Citizenship: Italian

Inventor's Signature: Francesco Tedesco
(if not contained in the request, or if declaration is corrected or added under Rule 26*ter* after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 24 July 2003
(of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26*ter* after the filing of the international application)

**Name:** Roberto MARZARI

Residence: TRIESTE – ITALY
(city and either US state, if applicable, or country)

Mailing Address: Via Dei Berlam 9 – 34136 TRIESTE – ITALY

Citizenship: Italian

Inventor's Signature: Roberto Marzari
(if not contained in the request, or if declaration is corrected or added under Rule 26*ter* after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 24 July 2003
(of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26*ter* after the filing of the international application)

☐ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".

PATENT
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Certificate of Mailing: Date of Deposit: January 11, 2005 Label Number: EV 272783489 US

I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as **"Express Mail Post Office to Addressee"** with sufficient postage on the date indicated above and is addressed to Mail Stop PCT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Elvis De La Cruz
Printed name of person mailing correspondence

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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|---|---|---|---|
| Applicant: | Francesco Tedesco et al. | Art Unit: | Not Yet Assigned |
| Serial No.: | Not Yet Assigned | Examiner: | Not Yet Assigned |
| Deposited: | January 11, 2005 | Customer No.: | 21559 |
| Title: | Antibodies Anti-C5 Component of the Complement System and Their Use | | |

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PRELIMINARY AMENDMENT

Prior to examination, applicants request that the above-captioned patent application be amended as follows.

## AMENDMENT TO THE SPECIFICATION

Please add the following paragraph to page one of the application, after the title of the invention.

This application is a U.S. national stage application under 35 U.S.C. § 371 of PCT/EP2003/007487, filed July 10, 2003, which claims priority from Italian application number MI2002A001527, filed July 11, 2002.

## AMENDMENTS TO THE CLAIMS

1-36. (Canceled).

37. (New) A human antibody having specificity for the activated C5 component of the complement system characterised in that it recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b.

38. (New) Antibody according to claim 37 wherein said C5 component is of mammalian origin, chosen among: human, mouse, rat, and rabbit.

39. (New) Antibody according to claim 37 characterised in that it is recombinantly produced.

40. (New) Recombinant antibody according to claim 39, characterised in that it is in the form of single chain (scFv) comprising one variable region of the light chain covalently joined to one variable region of the heavy chain.

41. (New) Antibody according to claim 40, characterised by the fact that the light chain is a lambda chain, preferably Vλ3/V2-14 or a kappa chain, preferably Vκ4/DPK24, and the variable region of the heavy chain is the VH3 region, preferably VH3/V-48.

42. (New) Antibody according to claim 41, characterised in that it comprises at least one of the amino acid sequences selected from the group consisting of: SEQ ID NO:2, 4, and 6.

43. (New) Recombinant antibody according to claim 42 having amino acid sequence SEQ ID NO:6.

44. (New) Recombinant antibody according to claim 42 characterised in that it comprises both the amino acid sequences identified as SEQ ID NO:2 and SEQ ID NO:4, or their allelic variants or their conservative mutations.

45. (New) Recombinant antibody according to claim 42, characterised by the fact of comprising a polypeptide having at least 95% homology with at least one of the amino acid sequences corresponding to sequence SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

46. (New) Recombinant antibody according to claim 42 characterised in that it comprises at least one of the sequences selected from the group consisting of SEQ ID NO:2, 4, and 6 in combination with a sequence derived from an immunoglobulin heavy chain constant region.

47. (New) Recombinant antibody according to claim 46 wherein said immunoglobulin heavy chain constant region is selected from the group consisting of: human IgA heavy chain, human IgG heavy chain, murine heavy gamma chain, and rattus norvegicus heavy chain.

48. (New) Recombinant antibody according to claim 47 characterised in that it is dimeric.

49. (New) Recombinant chimeric protein characterised in that it comprises at least one of the sequences corresponding to SEQ ID NO: 2, 4, 6, 8, 10, or 12, or protein sequences having at least 95% homology with said sequences.

50. (New) Isolated nucleotide sequence encoding for the antibody according to claim 37.

51. (New) Nucleotide sequence according to claim 50 characterised in that it comprises at least one of the sequences selected from: SEQ ID NO:1, 3, and 5 or each one of SEQ ID NO:7, 8, and 9.

52. (New) Vector comprising a nucleotide sequence according to claim 51.

53. (New) Vector according to claim 52 characterised by the fact of being expression vectors in bacteria, yeasts, or higher eukaryotic cells.

54. (New) Isolated cell characterised by being transformed with the nucleotide sequence according to claim 51 or by the vector according to claim 52.

55. (New) Non-human transgenic animal, characterised by the fact of expressing nucleotide sequences according to claim 51.

56. (New) A pharmaceutical composition comprising as the active principle any one of the antibodies selected from the group consisting of:

- an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- an antibody comprising an amino acid sequences selected from the group consisting of: SEQ ID NO:2, 4, and 6, or each one of SEQ ID NO:7, 8 , and 9; and
- an antibody with at least 95% homology with at least one of the amino acid sequences corresponding to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6,

in combination with suitable excipients and/or diluents.

57. (New) A pharmaceutical composition comprising as the active principle any one of the nucleotide sequences selected from the group consisting of:

- a nucleotide sequence encoding an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- a nucleotide sequence comprising any one and at least one of the sequence selected from group consisting of SEQ ID NO:1, 3, and 5 or each one of SEQ ID NO:7, 9, and 11; and

- a nucleotide sequence encoding for an antibody at least 95% homologous to any one of the amino acid sequences selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6,

in combination with suitable excipients and/or diluents.

58. (New) The composition according to claim 56 for treating myocardium damage from reperfusion after ischaemia.

59. (New) The composition according to claim 57 for treating myocardium damage from reperfusion after ischaemia.

60. (New) A therapeutic method for the prevention or the treatment of diseases involving hyperactivation of the complement system to a patient in need thereof comprising administering to said subject a therapeutically effective amount of an antibody selected from the group consisting of:

- an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- an antibody comprising an amino acid sequences selected from the group consisting of: SEQ ID NO:2, 4, and 6, or each one of SEQ ID NO:7, 8, and 9; and
- an antibody with at least 95% homology with at least one of the amino acid sequences corresponding to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

61. (New) A therapeutic method for the prevention or the treatment of diseases involving hyperactivation of the complement system to a patient in need thereof comprising administering to said subject a therapeutically effective amount of a nucleotide sequence selected from the group consisting of:

- a nucleotide sequence encoding an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of

human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;

- a nucleotide sequence comprising any one and at least one of the sequence selected from group consisting of: SEQ ID NO:1, 3, and 5 or each one of SEQ ID NO: 7, 9, and 11; and
- a nucleotide sequence encoding for an antibody at least 95% homologous to any one of the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6.

62. (New) The therapeutic method according to claim 60 wherein said hyperactivation leads to a chronic or an acute inflammatory disease.

63. (New) The therapeutic method according to claim 61 wherein said hyperactivation leads to a chronic or an acute inflammatory disease.

64. (New) The therapeutic method according to claim 62 wherein said acute inflammatory disease is Multiple Organ Failure or myocardial infarction.

65. (New) The therapeutic method according to claim 63 wherein said acute inflammatory disease is Multiple Organ Failure or myocardial infarction.

66. (New) The therapeutic method according to claim 62 wherein said chronic inflammatory disease is selected from the group consisting of: rheumatoid arthritis, glomerulonephritis, multiple sclerosis, demyelinating peripheral neuropathies, and atherosclerosis.

67. (New) The therapeutic method according to claim 63 wherein said chronic inflammatory disease is selected from the group consisting of: rheumatoid arthritis, glomerulonephritis, multiple sclerosis, demyelinating peripheral neuropathies, and atherosclerosis.

68. (New) A method for setting up an animal model for a disease caused by hyperactivation of the complement system which comprises treating an animal with any one of the antibodies selected from the group consisting of:

- an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- an antibody comprising an amino acid sequences selected from the group consisting of: SEQ ID NO:2, 4, and 6, or each one of SEQ ID NO:7, 8, and 9; and
- an antibody with at least 95% homology with at least one of the amino acid sequences corresponding to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

69. (New) A method for setting up an animal model for a disease caused by hyper-activation of the complement system which comprises treating an animal with any one of the nucleotide sequences selected from the group consisting of:

- a nucleotide sequence encoding an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said anitbody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- a nucleotide sequence comprising any one and at least one of the sequence selected from group consisting of: SEQ ID NO:1, 3, or 5 or each one of SEQ ID NO: 7, 9, and 11; and
- a nucleotide sequence encoding for an antibody at least 95% homologous to any one of the amino acid sequence selected from the group consisting of to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

70. (New) Process for selecting anti-C5 antibodies endowed with the ability of inhibiting the formation of C5a from C5, comprising a first selection step on C5 antigen and a second selection step by means of inhibition of a hemolytic assay on SRBC.

71. (New) Process for the preparation of a recombinant antibody specific for the activated C5 component of the complement system and recognizing a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b, wherein is used any one of the isolated nucleotide sequences selected from the group consisting of:

- a nucleotide sequence comprising any one of the sequence selected from group consisting of: SEQ ID NO:1, 3, and 5 and each one of SEQ ID NO:7, 9, and 11; and
- a nucleotide sequence encoding for an antibody at least 95% homologous to any one of the amino acid sequence selected from the group consisting of: SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

72. (New) Kit comprising any one of the antibodies selected from the group consisting of:

- an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK (SEQ ID NO:15) and wherein said antibody inhibits the conversion of the C5 alpha chain to C5a and C5b;
- an antibody comprising an amino acid sequences selected from the group consisting of: SEQ ID NO:2, 4, and 6, or each one of SEQ ID NO:7, 8, and 9;
- an antibody with at least 95% homology with at least one of the amino acid sequences corresponding to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

73. (New) Kit comprising any one of the nucleotide sequences selected from the group consisting of:

- a nucleotide sequence encoding an antibody against the activated C5 component of the complement system which recognises a polypeptide having at least 80% homology with the peptide comprising the region corresponding to sequence 731-740 of the C5 component of human complement, said peptide having the sequence KDMQLGR↓LHMKTLLPVSK

(SEQ ID NO:15) and wherein said anitbody inhibits the conversion of the C5 alpha chain to C5a and C5b;

- a nucleotide sequence comprising any one and at least one of the sequences selected from group consisting of SEQ ID NO:1, 3, and 5 and each one of SEQ ID NO:7, 9, and 11; and
- a nucleotide sequence encoding an antibody at least 95% homologous to any one of the amino acid sequences selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6.

74. (New) A process for the selection of inhibitors of the conversion of the C5 component of activated complement to its biologically active fragments, characterised by the use of an antibody according to claim 37.

75. (New) A peptide with the amino acid sequence: KDMQLGRLHMKTLLPVSK (SEQ ID NO:15).

76. (New) A process for the selection of inhibitors of the conversion of the C5 component of activated complement to its biologically active fragments, wherein the peptide according to claim 75 is used.

## CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. No new matter is added by the present amendment. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: January 11, 2005

Susan M. Michaud

Susan M. Michaud, Ph.D.
Reg. No. 42,885

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045

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Date of Deposit: January 11, 2005 Label Number: EV 272783489 US

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Elvis De La Cruz

Printed name of person mailing correspondence

Signature of person mailing correspondence

Substitute Form PTO 1390 U.S. Department of Commerce Patent and Trademark Office

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. § 371

Attorney Docket Number: 50294/016001

U.S. Application Number: Not Yet Assigned

| INTERNATIONAL APPLICATION NUMBER | INTERNATIONAL FILING DATE | PRIORITY DATE CLAIMED |
|---|---|---|
| PCT/EP2003/007487 | July 10, 2003 | July 11, 2002 |

| | |
|---|---|
| TITLE OF INVENTION: | Antibodies Anti-C5 Component of the Complement System and Their Use |
| APPLICANTS FOR DO/EO/US: | Francesco Tedesco and Roberto Marzari |

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

| | |
|---|---|
| 1. | ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. § 371. |
| 2. | ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. § 371. |
| 3. | ☒ This is an express request to begin national examination procedures (35 U.S.C. § 371(f)). |
| 4. | ☐ The U.S. has been elected. |
| 5. | A copy of the International Application (35 U.S.C. § 371(c)(2)).<br>☒ a. is transmitted herewith (required only if not transmitted by the International Bureau).<br>☐ b. has been transmitted by the International Bureau.<br>☐ c. Is not required, as the application was filed with the United States Receiving Office (RO/US). |
| 6. | An English language translation of the International Application into English (35 U.S.C. § 371(c)(2)).<br>☐ a. is transmitted herewith.<br>☐ b. has been previously submitted under 35 U.S.C. 154(d)(4). |
| 7. | Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. § 371(c)(3)).<br>☐ a. are transmitted herewith (required only if not transmitted by the International Bureau).<br>☐ b. have been transmitted by the International Bureau.<br>☐ c. have not been made; however, the time limit for making such amendments has NOT expired.<br>☒ d. have not been made and will not be made. |
| 8. | ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. § 371(c)(3)). |
| 9. | ☒ An oath or declaration of the inventors (35 U.S.C. § 371(c)(4)). |
| 10. | ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371 (c)(5). |
| 11. | ☐ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98. |
| 12. | ☒ An assignment for recording. A separate cover sheet in compliance with 37 C.F.R. §§ 3.28 and 3.31 is included. |
| 13. | ☒ A preliminary amendment. |
| 14. | ☐ A substitute specification. |
| 15. | ☐ A power of attorney and/or change of address letter (combined with inventor declaration). |
| 16. | ☐ Request for Deferred Examination. |
| 17. | ☐ Application Data Sheet. |
| 18. | ☒ Other items or information: transmittal of drawings. |

| | | | | | |
|---|---|---|---|---|---|
| 19. | ⊠ The following fees are submitted: | | | | |
| Basic National Stage Fee $300 | | | | $300 | |
| National Stage Search Fee: $500 | | | | $500 | |
| National Stage Examination Fee: $200 | | | | $200 | |
| Surcharge of $130 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 C.F.R. § 1.492(e)). | | | | $0 | |
| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE | | |
| Total claims | 40 - 20 = | 20 | x $50 | $1000 | |
| Independent claims | 13 - 3 = | 10 | x $200 | $2000 | |
| Multiple dependent claims (if applicable) | | | + $360 | $0 | |
| Application Size Fee: Additional fee for specification and drawings in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is $250 for each additional 50 sheets of paper or fraction thereof. | | | | | |
| TOTAL SHEETS | EXTRA SHEETS | Number of each additional 50 sheets or fraction thereof (round up to a whole number) | RATE | | |
| -100=- | 0/50= | 0 | X$250 | $0 | |
| | | | TOTAL OF ABOVE CALCULATIONS = | $4000 | |
| Reduction of 1/2 for filing by small entity, if applicable. Applicant claims small entity status under 37 C.F.R. § 1.27. | | | | $2000 | |
| | | | SUBTOTAL = | $2000 | |
| Processing fee of $130.00 for furnishing the English translation later than 30 months from the earliest claimed priority date (37 C.F.R. § 1.492(f)). + | | | | $0 | |
| | | | TOTAL NATIONAL FEE = | $2000 | |
| Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. §§ 3.28, 3.31). $40.00 per property. + | | | | $40 | |
| | | | TOTAL FEES ENCLOSED = | $2040 | |
| | | | | Amount to be refunded | $ |
| | | | | charged | $ |

⊠ a. A check in the amount of $2040 to cover the above fees is enclosed.
□ b. Please charge my Deposit Account No. 03-2095 in the amount of $ [**] to cover the above fees.
⊠ c. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 03-2095.

NOTE: Where an appropriate time limit under 37 C.F.R. §§ 1.494 or 1.495 has not been met, a petition to revive (37 C.F.R. § 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Susan M. Michaud, Ph.D.
Clark & Elbing LLP
101 Federal Street
Boston, MA 02110-2214

Telephone: 617-428-0200
Facsimile: 617-428-7045
Customer No.: 21559

Susan M. Michaud
Signature

Susan M. Michaud, Ph.D.
Reg. No. 42,885